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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/721,543	11/21/2000	Fenyong Liu	BERK-005	2657

24353 7590 07/21/2003

BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD RD
SUITE 200
MENLO PARK, CA 94025

EXAMINER
NGUYEN, QUANG

ART UNIT	PAPER NUMBER
1636	17

DATE MAILED: 07/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/721,543	LIU ET AL.	
	Examiner	Art Unit	
	Quang Nguyen, Ph.D.	1636	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 June 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *25 June 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☒ The proposed amendment(s) will not be entered because:

(a) ☒ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: *See Continuation Sheet*.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet*.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☒ will not be entered or b)☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1,6,8,10,12-16,19,21,23,25 and 26*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☐ Other: _____

DAVID GUZO
PRIMARY EXAMINER

Continuation of 2. NOTE: The newly amended claims 6, 12-14, 16, 15, 16, 19, 23 and 25-26 raise a new ground of rejection, specifically under 35 U.S.C. 112, second paragraph. For example, the lack of antecedent basis for the limitations "said RNA" in the proposed claim 6, "composition" in proposed claims 12-14, "said polynucleotide" in the proposed claim 15, and "said antiviral polynucleotide" in the proposed claim 16. Additionally, the scope of the amended claims 6 and 8 is not the same as the scope of the finally rejected claims. This is because the polynucleotide ligand in the proposed claims 6 and 8 is not required to possess an anti-hCMV activity.

Continuation of 5. does NOT place the application in condition for allowance because: Applicants' arguments are not found to be persuasive for the reasons discussed below and that these have been discussed more extensively in the Final Office Action.

(1) With respect to the Written Description rejection, Applicants argue that a representative number of species has been provided, and that three separate examples of sequences (L13, L19 and L66) have demonstrated anti-viral activity. Additionally, specific xamples of polynucleotide ligands meeting the requirements of the claims are provided in Tables 1 and 2.

Please note that apart from the sole disclosure of the L19 ligand having SEQ ID NO:12 and the ability to block hCMV entry into targeted cell via its specific binding to hCMV envelope glycoprotein gB in the elected group of RNA polynucleotide ligand sequences, th instant specification fails to disclose a representative number of RNA polynucleotide ligands that have hCMV antiviral activity via the binding of any hCMV envelope or capsid proteins, particularly for a broad genus of elected RNA polynucleotide ligands of from 15 to 100 nucleotides in length that share sequence similarity or common core structure to any of SEQ ID NOs:12-16. Additionally, apart from th common functional limitation of binding to a hCMV and inhibiting hCMV infection, the specification fails to disclose or identify the relevant structural characteristics or common essential core elements that are responsible for the desired functions, not even for the L19 ligand, let alone for any other RNA ligands of from 15 to 100 nucleotides in length. What are the sequences (necessary for a proper 3-dimensional folding or by other means) that these RNA ligands need to possess in order for them to exhibit an anti-hCMV activity? It is also noted that there is no direct correlation between the ability of an RNA polynucleotide ligand that binds to hCMC and its ability to block hCMV entry into a cell as evidenced by the teachings of the present application for the ligands L17 and L31 (see examples 1 and 2 of the instant specification). Furthermore, adequate written description requires more than a mere statement that it is part of th invention and reference to a potential method of isolating it, and that the Written description provision is severable from its Enablement provision.

(2) With respect to the scope of Enablement rejection, Applicants argue that the sequences of SEQ ID NO:12-16 meet the requirements of 35 U.S.C. 112 as evidenced by the statements "In our study, the selected ligands exhibited a high affinity to hCMV particles and were highly effective in inhibiting viral production" and "the binding affinity of the ligands also appeared to correlate with th ir activity in inhibiting viral infection". Applicants further argue that the ligands cited by Examiner that lack antiviral activity are unrelated to the presently claimed invention because the presently claimed sequences share specific sequence motifs, e.g., the terminal TGGG sequence, and the internal motif purine-CCC(AT/TA) as well as other similarities, and therefore these sequences should also have antiviral activity.

Please note the cited statement "the binding affinity of the ligands also APPEARED to correlate with their activity in inhibiting viral infection". Additionally, there is no objective evidence of record indicating or suggesting that the sequence motifs: TGGG sequence, the internal motif purine-CCC(AT/TA) are essential for the binding of the L19 ligand to the hCMV glycoprotein gB that blocks effectively hCMV entry into targeted cells. Although the ligands L17 and L31 do not fall within the elected group of RNA polynucleotide ligand sequences, they demonstrate that simply binding to hCMV does not necessarily lead to the inhibition of hCMV entry into targeted cells. This supports the Examiner's position that the anti-hCMV activity has to be detemined empirically, and that there is no way to predict which nucleotide modification (addition, deletion, substitution) at which nucleotide position and in which combinations to the ligand L19 having SEQ ID NO:12 would or would not result in the RNA polyncleotide ligand variants possessing the desired anti-hCMV activity. Furthermore, the courts have stated that reasonable correlation must exist between scope of exclusive right to patent application and scope of enablement set forth in the patent application.